PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 5185-PCT	FOR FURTHER ACTION	See Form PCT/IPEA/416
International application No. PCT/US04/41883	International filing date *(day/month/year)* 10 December 2004 (10.12.2004)	Priority date *(day/month/year)* 12 December 2003 (12.12.2003)
International Patent Classification (IPC) or national classification and IPC IPC: **C12Q 1/68**(2007.01);**C07H 21/04**(2007.01) USPC: 435/6,91.2		
Applicant BAYER PHARMACEUTICALS CORPORATION		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 7 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☐ *(sent to the applicant and to the International Bureau)* a total of ___ sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) _____ , containing a sequence listing and/or tables related thereto, in electronic form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).
4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☐	Box No. II	Priority
☐	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☒	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
29 June 2005 (29.06.2005)	06 December 2006 (06.12.2006)
Name and mailing address of the IPEA/ US Mail Stop PCT, Attn: IPEA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (571) 273-3201	Authorized officer Valerie Bell-Harrison Sarae Bausch Telephone No. (571)272-1600

Form PCT/IPEA/409 (cover sheet)(April 2005)

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
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Box No. I Basis of the report

1. With regard to the **language**, this report is based on:

☒ the international application in the language in which it was filed.

☐ a translation of the international application into English, which is the language of a translation furnished for the purposes of:

☐ international search (under Rules 12.3 and 23.1(b))

☐ publication of the international application (under Rule 12.4(a))

☐ international preliminary examination (under Rules 55.2(a) and/or 55.3(a))

2. With regard to the **elements** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

☒ the international application as originally filed/furnished

☒ the description:
pages 1-45 as originally filed/furnished
pages* NONE received by this Authority on _____
pages* NONE received by this Authority on _____

☒ the claims:
pages 44-46 as originally filed/furnished
pages* NONE as amended (together with any statement) under Article 19
pages* NONE received by this Authority on _____
pages* NONE received by this Authority on _____

☒ the drawings:
pages NONE as originally filed/furnished
pages* NONE received by this Authority on _____
pages* NONE received by this Authority on _____

☒ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____
☐ the claims, Nos. _____
☐ the drawings, sheets/figs _____
☐ the sequence listing (*specify*): _____
☐ any table(s) related to the sequence listing (*specify*): _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

☐ the description, pages _____
☐ the claims, Nos. _____
☐ the drawings, sheets/figs _____
☐ the sequence listing (*specify*): _____
☐ any table(s) related to the sequence listing (*specify*): _____

* *If item 4 applies, some or all of those sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

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Box No. IV Lack of unity of invention

1. ☒ In response to the invitation to restrict or pay additional fees the applicant has, within the applicable time limit:

   ☒ restricted the claims.

   ☐ paid additional fees.

   ☐ paid additional fees under protest, and, where applicable, the protest fee

   ☐ paid additional fees under protest but the applicable protest fee was not paid

   ☐ neither restricted the claims nor paid additional fees

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is:

   ☐ complied with.

   ☒ not complied with for the following reasons:

Please See Continuation Sheet

4. Consequently, this report has been established in respect of the following parts of the international application:

   ☐ all parts

   ☒ the parts relating to claims Nos. 1-15 SEQ ID No. 1

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

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Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims NONE	YES
	Claims 1-15	NO
Inventive Step (IS)	Claims NONE	YES
	Claims 1-15	NO
Industrial Applicability (IA)	Claims 1-15	YES
	Claims NONE	NO

2. Citations and Explanations (Rule 70.7)

Claims 1-15 lack inventive step under PCT Article 33(3) as being anticipated by Choe et al. who teaches the claimed method of determining the level of expression of one or more genes between different samples wherein the one or more genes are selected from nucleotides SEQ ID No. 1-19 and polypeptides 20-37.

Claims 1-15 the criteria set out in PCT Article 33(4), and thus claim 1-15 industrial applicability because the subject matter claimed can be made or used in industry.

---------- NEW CITATIONS ----------

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Supplemental Box Relating to Sequence Listing

Continuation of Box No. I, item 2:

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this report was established on the basis of:

   a. type of material

   ☒ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material

   ☒ on paper

   ☒ in electronic form

   c. time of filing/furnishing

   ☒ contained in the international application as filed

   ☒ filed together with the international application in electronic form

   ☐ furnished subsequently to this Authority for the purposes of search and/or examination

   ☐ received by this Authority as an amendment* on _____

2. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

* *If item 4 in Box No. I applies, the listing and/or table(s) related thereto, which form part of the basis of the report, may be marked "superseded."*

Supplemental Box

In case **the space in any of the preceding boxes is not sufficient.**

Continuation of:

IV. 3. This Authority considers that the requirement of unity of invention is accordance with Rules 13.1, 13.2 and 13.3 is not complied with for the following reasons:
This application contains the following inventions or groups of inventions, which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group 1, claim(s) 1-15, drawn to method of determining the level of expression of one or more genes between different examples wherein the one or more genes are selected from nucleotides SEQ ID No. 1-19 and polypeptides 20-37.

Group 2, claim(s) 16-19, drawn to kits and an array comprising probes from the genes enumerated in SEQ ID No. 1-19 and polypeptides SEQ ID No. 20-37.

Group 3, claim(s) 20-22, drawn to test kit comprising an antibody that specifically binds a polypeptide selected from SEQ ID No. 20-37.

Further species election:

For group 1-3, the species of the groups are considered each of the 19 separately recited sequences for the polynucleotides and 18 separately recited amino acids that correspond to the gene or gene products being measured in the method of group I recited in SEQ ID No. 1-19 and correspond to SEQ ID No. 20-37.

The first named invention which will be searched is Group 1, claims 1-15 with respect to SEQ ID No. 1 as it relates to the method of group I.

The inventions listed as Groups 1-3 do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: the technical features that joins all these inventions is that they encompass steps that involve the detection of gene expression involved in the detection of cancer. However, a method of detecting differentially expressed genes in cancer was known at the time the invention was made and thus, this is not a special technical feature in view of the PCT rules. In addition, SEQ ID no. 1 that represents the special technical feature of Group II, also know as GenBank ID NM_000177, was also known in the prio art (see JM (2002) 324, 691-702). Group I is the first named invention including a method of determining the level of expression of one or more genes between different samples. Group II is drawn to kits and an array comprising probes from the genes enumerated in SEQ ID No. 1-19. However, not only are each of these special technical features of group I and II not the same and shared between the two groups, they were also both already known in the prior art. There is no special technical feature that joins the first named method and first named product as the product and the method of group I is anticipated in the prior art. For example, Us Patent publication 2002/004239 A1 by Kaufman et al. teach a method of detecting genes differentially expressed in breast cancer and therefore teach the special technical feature of group I. The remaining groups include

Supplemental Box

additional products and methods that are no linked by a unifying inventive concept as they are drawn to unique products and methods and are so separately grouped.

The species listed above do not related to single general inventive concept under PCT Rule 13.1, because under PCT Rule 13.2, the species lack the same or corresponding special technical feature for the following reasons: each is drawn to a unique nucleic acid sequence that does not share a common structure with the others. In addition, each nucleic acid, polypeptide, and antibody, all consist of different physical structures. For example, while the polynucleotides are composed of a chain of nucleic acids linked by a phosphodiester bond the polypeptides are compose of amino acids linked in a peptide bond and arranged spatially in a number of different tertiary structures include alpha helices, beta-pleated sheets, and hydrophobic loops. Furthermore, the antibody of Group III is composed of amino acids linked in peptide bonds arranged spatially in very specific tertiary structure that allows that antibody to specifically bind to particular regions, i.e. epitopes of the encoded polypeptides. Further, antibodies are glycosated and their tertiary structure is unique, where four units (2 light chains 2 heavy chains) associated via disulfide bonds into a Y-shaped symmetric dimer. As a result each is a different structure and do not relate to a single general inventive concept. .